AMENDMENTS TO THE CLAIMS

1-7. *(Cancelled)*

8. *(Currently Amended)* ~~The method of claim 7,~~ A computer-aided method of docking a ligand to a protein so as to determine ligand conformations likely to bind to said protein, said method comprising:

performing a pre-docking conformational search and generating multiple solution conformations of a ligand therefrom;

generating a binding site image of a protein, said binding site image comprising multiple hot spots;

matching hot spots of the binding site image to atoms in at least one conformation of the multiple solution conformations of the ligand to initially position said at least one conformation of said ligand as a rigid body into said binding site so as to obtain at least one position of the ligand relative to the protein in a protein-ligand complex;

optimizing the at least one position of the ligand while allowing translation, orientation and rotatable bonds of the ligand to vary, and while holding the protein fixed;

calculating a score for the optimized position of the ligand using one or more potential functions;

selecting one or more optimized ligand positions based on said score;

wherein said matching comprises:

matching atoms of the at least one solution conformation of the ligand to appropriate hot spots of the protein by positioning the at least one solution conformation of the ligand as a rigid body into the binding site image;

defining a match, said match determining a unique rigid body transformation; and

using the unique rigid body transformation to place the at least one solution conformation of the ligand into the binding site of the protein; and

wherein said determining the unique rigid body transformation comprises determining the unique rigid body transformation that minimizes:

$$I(R,T) = \sum_{j=1}^{3} \left| H_j - RA_j - T \right|^2$$

where:

$I(R,T)$ = rms deviation between a j^{th} hot spot and a j^{th} atom of the at least one solution conformation of the ligand;

H_j = a position vector of a j^{th} hot spot of the protein;

A_j = a position vector of a j^{th} atom of the at least one solution conformation of the ligand;

R = a 3x3 rotation matrix; and

T = a translation vector.

9-27. ***(Cancelled)***

28. ***(Previously Presented)*** ~~The at least one program storage device of claim 27,~~ At least one program storage device readable by a machine, tangibly embodying at least one program of instructions executable by the machine to perform a method of docking a ligand to a protein so as to determine ligand conformations likely to bind to said protein, said method comprising:

performing a pre-docking conformational search and generating multiple solution conformations of a ligand therefrom;

generating a binding site image of a protein, said binding site image comprising multiple hot spots;

matching hot spots of the binding site image to atoms in at least one conformation of the multiple solution conformations of the ligand to initially position said at least one conformation of said ligand as a rigid body into said binding site so as to obtain at least one position of the ligand relative to the protein in a protein-ligand complex;

optimizing the at least one position of the ligand while allowing translation, orientation and rotatable bonds of the ligand to vary, and while holding the protein fixed;

calculating a score for the optimized position of the ligand using one or more potential functions;

selecting one or more optimized ligand positions based on said score;

wherein said matching comprises:

matching atoms of the at least one solution conformation of the ligand to appropriate hot spots of the protein by positioning the at least one solution conformation of the ligand as a rigid body into the binding site image;

defining a match, said match determining a unique rigid body transformation; and

using the unique rigid body transformation to place the at least one solution conformation of the ligand into the binding site of the protein; and

wherein said determining the unique rigid body transformation comprises determining the unique rigid body transformation that minimizes:

$$I(R,T) = \sum_{j=1}^{3} \left| H_j - RA_j - T \right|^2$$

where:

I(R,T) = rms deviation between a j^{th} hot spot and a j^{th} atom of the at least one solution conformation of the ligand ;

H_j = a position vector of a j^{th} hot spot of the protein;

A_j = a position vector of a j^{th} atom of the at least one solution conformation of the ligand;

R = a 3x3 rotation matrix; and

T = a translation vector.

29-30. ***(Cancelled)***